

-- A modified SCID mouse model was used because it is known that severe combined immunodeficiency scid/scid (SCID) mice, C.B.-17 (Bosma et al., *Nature*, 301:527 (1983)) reconstituted with human peripheral blood mononuclear cells (hu-PBMC-SCID) can produce significant quantities of human immunoglobulins (Ig) (~~Moiser~~ Mosier et al., *Nature*, 335:256 (1988); ~~Moiser~~ Mosier et al., *J. Clin. Immunol.*, 10:185 (1990); Abedi et al., *J. Immunol.*, 22:823 (1992); and Mazingue et al., *Eur. J. Immunol.*, 21:1763 (1991).) The predominant isotype of human immunoglobulin (Ig) produced in hu-PBMC-SCID mice is IgG. Generally, IgM, IgA and IgE isotypes are found in very low or non-detectable levels except in cases where PBMC is obtained from donors with certain autoimmune or allergic disease conditions. It has also been reported that manipulation of hu-PBMC SCID mouse model with certain cytokines may be provided for the generation of significant levels of non-IgG isotypes, including IgE (Kilchherr et al., *Cellular Immunology*, 151:241 (1993); Spiegelberg et al., *J. Clin. Investigation*, 93:711 (1994); and Carballido et al., *J. Immunol.*, 155:4162 (1995)). The hu-PBMC-SCIDs, has been also used to generate antigen specific Ig provided the donor has been primed for the antigen *in vivo*. --

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 38: (previously amended) A method of inhibiting production of IgE in a human subject with an IgE-mediated allergic disorder comprising parenterally administering an IgE production inhibiting amount of an anti-human CD23 monoclonal antibody comprising a human gamma-1 constant region;

which antibody competes for binding to CD23 with an antibody comprising the complementarity-determining regions CDR1, CDR2, and CDR3 of the light and heavy chains of antibody 6G5 or of antibody 5E8; wherein

CDR1, CDR2, and CDR3 of the light chain of antibody 6G5 are the polypeptides encoded by nucleotides 124-165, 211-231, and 328-357, respectively, of SEQ ID NO. 1;

CDR1, CDR2, and CDR3 of the heavy chain of antibody 6G5 are the polypeptides encoded by nucleotides 148-165, 208-258, and 355-390, respectively, of SEQ ID NO. 3;

CDR1, CDR2, and CDR3 of the light chain of antibody 5E8 are the polypeptides encoded by nucleotides 136-168, 214-234, and 331-357, respectively, of SEQ ID NO. 5; and

CDR1, CDR2, and CDR3 of the heavy chain of antibody 5E8 are the polypeptides encoded by nucleotides 148-168, 211-261, and 358-378, respectively, of SEQ ID NO. 7.

Claim 39: (previously amended) The method of Claim 38, wherein the anti-human CD23 monoclonal antibody that is administered comprises the complementarity-determining regions CDR1, CDR2, and CDR3 of the light and heavy chains of an antigen binding portion of a primate anti-human CD23 antibody.

Claim 40: (previously amended) The method of Claim 38, wherein the anti-human CD23 monoclonal antibody that is administered is a human gamma-1 monoclonal antibody.

Claim 41: (previously amended) The method of Claim 38, wherein the anti-human CD23 monoclonal antibody that is administered comprises an antigen-binding portion of a rodent anti-human CD23 antibody.

Claim 42: (previously amended) The method of Claim 38, wherein the anti-human CD23 monoclonal antibody that is administered is a humanized antibody.

Claim 43: (previously amended) The method of Claim 38, wherein the anti-human CD23 monoclonal antibody that is administered inhibits production of IgE *in vitro*.

Claim 44: (previously amended) The method of Claim 43, wherein the anti-human CD23 monoclonal antibody that is administered inhibits IL-4 induced production of IgE by B cells *in vitro*.

Claim 45: (previously amended) The method of Claim 38, wherein the anti-human CD23 monoclonal antibody that is administered inhibits IL-4 induced production of IgE *in vivo*.

Claim 46: (previously amended) The method of Claim 39, wherein the anti-human CD23 monoclonal antibody that is administered comprises the complementarity-determining regions CDR1, CDR2, and CDR3 of the light and heavy chains of antibody 6G5 or of antibody 5E8; wherein

CDR1, CDR2, and CDR3 of the light chain of antibody 6G5 are the polypeptides

encoded by nucleotides 124-165, 211-231, and 328-357, respectively, of SEQ ID NO. 1;

CDR1, CDR2, and CDR3 of the heavy chain of antibody 6G5 are the polypeptides encoded by nucleotides 148-165, 208-258, and 355-390, respectively, of SEQ ID NO. 3;

CDR1, CDR2, and CDR3 of the light chain of antibody 5E8 are the polypeptides encoded by nucleotides 136-168, 214-234, and 331-357, respectively, of SEQ ID NO. 5; and

CDR1, CDR2, and CDR3 of the heavy chain of antibody 5E8 are the polypeptides encoded by nucleotides 148-168, 211-261, and 358-378, respectively, of SEQ ID NO. 7.

Claim 47: (previously amended) A method of treating an IgE mediated allergic disorder in a human subject comprising parenterally administering a therapeutically effective amount of an anti-human CD23 monoclonal antibody comprising a human gamma-1 constant region; which antibody competes for binding to CD23 with an antibody comprising the complementarity-determining regions CDR1, CDR2, and CDR3 of the light and heavy chains of antibody 6G5 or of antibody 5E8; wherein

CDR1, CDR2, and CDR3 of the light chain of antibody 6G5 are the polypeptides encoded by nucleotides 124-165, 211-231, and 328-357, respectively, of SEQ ID NO. 1;

CDR1, CDR2, and CDR3 of the heavy chain of antibody 6G5 are the polypeptides encoded by nucleotides 148-165, 208-258, and 355-390, respectively, of SEQ ID NO. 3;

CDR1, CDR2, and CDR3 of the light chain of antibody 5E8 are the polypeptides encoded by nucleotides 136-168, 214-234, and 331-357, respectively, of SEQ ID NO. 5; and

CDR1, CDR2, and CDR3 of the heavy chain of antibody 5E8 are the polypeptides encoded by nucleotides 148-168, 211-261, and 358-378, respectively, of SEQ ID NO. 7.

Claim 48: (previously amended) The method of claim 47, wherein the anti-human CD23 monoclonal antibody that is administered is selected from the group consisting of a human gamma-1 antibody, an antibody comprising an antigen-binding portion of a rodent anti-human CD23 antibody, and an antibody comprising an antigen-binding portion of a primate anti-human CD23 antibody.

Claim 49: (previously amended) The method of claim 48, wherein the anti-human CD23 monoclonal antibody that is administered comprises the complementarity-determining regions CDR1, CDR2, and CDR3 of the light and heavy chains of antibody 6G5

or of antibody 5E8; wherein

CDR1, CDR2, and CDR3 of the light chain of antibody 6G5 are the polypeptides encoded by nucleotides 124-165, 211-231, and 328-357, respectively, of SEQ ID NO. 1;

CDR1, CDR2, and CDR3 of the heavy chain of antibody 6G5 are the polypeptides encoded by nucleotides 148-165, 208-258, and 355-390, respectively, of SEQ ID NO. 3;

CDR1, CDR2, and CDR3 of the light chain of antibody 5E8 are the polypeptides encoded by nucleotides 136-168, 214-234, and 331-357, respectively, of SEQ ID NO. 5; and

CDR1, CDR2, and CDR3 of the heavy chain of antibody 5E8 are the polypeptides encoded by nucleotides 148-168, 211-261, and 358-378, respectively, of SEQ ID NO. 7.

Claim 50: (previously amended) The method of any one of claims 47, 48 or 49, wherein said allergic disorder is selected from the group consisting of allergic rhinitis, allergic contact dermatitis, anaphylactic reactions, asthma, and bronchitis.

Claim 51 (currently amended): The method of any one of claims 47, 48, or 49, wherein parenteral administration includes subcutaneous, ~~intravascular~~ intravenous, intramuscular, rectal, vaginal and intraperitoneal administration.

Claim 52 (canceled)

Claim 53: (previously amended) The method of claim 51, wherein the antibody is administered by subcutaneous administration.

Claim 54: (previously amended) The method of claim 51, wherein the antibody is lyophilized for storage and reconstituted prior to administration.

Claim 55: (previously added) The method of Claim 39, wherein the anti-human CD23 monoclonal antibody that is administered comprises the variable regions of the light and heavy chains of antibody 6G5 having the sequences shown as amino acids 1-111 of SEQ ID NO: 2 and amino acids 1-122 of SEQ ID NO: 4, respectively.

Claim 56: (previously added) The method of claim 39, wherein the anti-human CD23 monoclonal antibody that is administered comprises the variable regions of the light and heavy chains of antibody 5E8 having the amino acid sequences shown as amino acids 1-107 of SEQ ID NO: 6 and amino acids 1-118 SEQ ID NO: 8, respectively.

Claim 57: (previously added) The method of claim 38, wherein said allergic disorder is selected from the group consisting of allergic rhinitis, allergic contact dermatitis, anaphylactic reactions, asthma, and bronchitis.

Claim 58: (previously added) The method of claim 38, wherein parenteral administration includes subcutaneous, intramuscular, intravenous, rectal, vaginal and intraperitoneal administration.

Claim 59: (previously added) The method of claim 58, wherein the antibody is administered by subcutaneous administration.

Claim 60: (previously added) The method of Claim 49, wherein the anti-human CD23 monoclonal antibody that is administered comprises the variable regions of the light and heavy chains of antibody 6G5 having the sequences shown as amino acids 1-111 of SEQ ID NO: 2 and amino acids 1-122 of SEQ ID NO: 4, respectively.

Claim 61: (previously added) The method of claim 49, wherein the anti-human CD23 monoclonal antibody that is administered comprises the variable regions of the light and heavy chains of antibody 5E8 having the amino acid sequences shown as amino acids 1-107 of SEQ ID NO: 6 and amino acids 1-118 SEQ ID NO: 8, respectively.

Claim 62 (currently amended): The method of claim 50, wherein parenteral administration includes subcutaneous, ~~intravascular~~ intravenous, intramuscular, rectal, vaginal and intraperitoneal administration.